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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,528	HOCHMAN, DARYL W.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,25-29,33,36,37,39-45,47-53 and 56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,25-29,33,36,37,39-45,47-53 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. By Amendment filed November 07, 2005, claims 35, 38, 46, 54 and 55 have been cancelled; claims 21, 36-37, 39-40, 42, 44-45, 47-51 and 53 have been amended; and claim 56 has been newly added. Claims 21, 25-29, 33, 36-37, 39-45, 47-53 and 56 are currently pending for prosecution on the merits.

Summary of Action

2. The rejection of the claim 45 under 35 U.S.C. 112, first paragraph, is not maintained in light of the amendment.

3. The rejection of the claims 21, 27-28, 36-37 and 45 as being anticipated by Mathew et al. (Neurology, 1996;46:1226-1230) is maintained for the reasons of record.

4. The rejection of the claims 25-26, 29, 33, 39-44 and 47-53 under 35 U.S.C. 103(a) as being unpatentable over Mathew et al. (Neurology, 1996;46:1226-1230), and further in view of Levin (US 6432986) and Bentley et al. (US 6369094) and Becker et al. (US 5256687) is maintained for the reasons of the record.

5. The provisional rejection of the claims 21, 25-29, 33 and 36-37, 39-45, 47-53 under the judicially created doctrine of double patenting over claims 12-18 of copending Application No. 11/101,000 is maintained for the reasons of record.

6. Applicant's amendment necessitates a new ground of rejection(s) in this Office Action.

Claim Objections

7. Claims 45 and 56 are objected to because of the following informalities: Improper Markush type language is used in claims 45 and 56. "...selected from the group consisting of: thiazide; and thiazide-like compositions" and "...selected from the group consisting of: bumetanide; and ethacrynic acid" should be corrected as "...selected from the group consisting of thiazide and thiazide-like compositions" and "...selected from the group consisting of bumetanide and ethacrynic acid" respectively.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 21, 27-28, 36-37, 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Mathew et al. (Neurology, 1996;46:1226-1230).

Mathew teaches use of acetazolamide and furosemide in combination with abortive antimigraine agents (e.g., ergotamine, DHE, or sumatriptan), prophylactic agents such as beta blockers, amitriptyline or methysergide and/or nonsteroidal anti-inflammatory agents for the treatment of chronic daily headache including migraine headache with or without aura in human (abstract; page 1226, column 2, para. 5 thru page 1228, column 1, para. 4 ; page 1228, column 2, para. 6 thru page 1229, column 1, para. 1; page 1229, column 2, para. 1). The reference discloses

that said combination resulted "in the number of days of severe headache, reduced consumption of abortive agents, and overall improvement of quality of life".

Although Mathew is silent about the functional characteristic of Na+K+2Cl- (i.e., furosemide) in "capable of inhibiting Na+K+2Cl- cotransport in glial cells to the central nervous system", "blocks spontaneous synchronized depolarizing oscillations of neuronal population activity in the central nervous system"; "produces modulation of the chloride concentration in extracellular space in the central nervous system", such characteristics or properties deems to be inherent to the of Na+K+2Cl- cotransporter antagonist such as furosemide. Therefore, the reference anticipates the claimed invention.

Although the amended claim 21 recite "consisting essentially of" language, the placement of "consisting essentially of" before "administering" does not limit Na+K+2Cl- as the sole active ingredient in the anti-migraine composition. Therefore, the referenced administration of the acetazolamide and furosemide in combination with the antimigraine agents, prophylactic agents and/or nonsteroidal anti-inflammatory agents for the treatment of migraine headache with or without aura by "reducing the number of days of severe headache...overall improvement of quality of life" anticipates the claimed invention.

9. Claims 21, 27-28, 36-37, 45, 48, 49 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by dePadova (US 5753651).

dePadova teaches use of AT1 receptor antagonist in combination with diuretics (i.e., furosemide, ethacrynic acid, bumetanide) for the treatment of acute or chronic pain mediated by sympathetic nervous system including menstrual migraine, wherein said composition is

administered in various dosage forms including time-release and/or delay release dosage forms (abstract; column 2, line 28; column 4, lines 31-36; column 9, lines 35-38; claims 1 and 13).

Although dePadova is silent about the functional characteristic of Na+K+2Cl- (i.e., furosemide, ethacrynicacid, bumetanide) in "capable of inhibiting Na+K+2Cl- cotransport in glial cells to the central nervous system", "blocks spontaneous synchronized depolarizing oscillations of neuronal population activity in the central nervous system"; "produces modulation of the chloride concentration in extracellular space in the central nervous system", such characteristics or properties deems to be inherent to the of Na+K+2Cl- cotransporter antagonist such as furosemide. Therefore, the reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 25-26, 29, 33, 41, 43 and 47-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathew et al. (Neurology, 1996;46:1226-1230), and further in view of Levin (US 6432986) and Bentley et al. (US 6369094) and Becker et al. (US 5256687).

The teaching of Mathew has been discussed in above 35 USC 102(b) rejection.

Levin is being supplied as a reference to demonstrate the routine knowledge in the art of delivering anti-migraine agents by intranasal and transdermal or topical administration (column 36, lines 31-38; column 9, lines 7-17; column 41, lines 40-43); sustained release formulation, liposome formulation (column 31, lines 22-31); by implantation or therapeutic device (column 39, lines 3-62). Levin also teaches the use of divalproex sodium for the treatment of migraine headache (column 35, lines 31-32 and column 36, lines 6-7).

Bentley is being supplied as a reference to demonstrate the routine knowledge in the art of delivering anti-migraine agents in various dosage forms including oral, intracvernosal, parenteral (i.e., intracranially), transdermal, ocular and topical administration or controlled released and fast dispersion formulation (column 3, line 8 thru column 4, line 60).

Becker is being supplied as a reference to demonstrate the routine knowledge in the art of using mannitol as pharmaceutical excipient or carrier for furosemide (column 11, line 13).

The teaching of Mathew differs from the claimed invention in (i) the incorporation of a blood brain barrier permeability enhancer or hyperosmotic agent or solution (claims 25-26, 33, 39, 40 and 53, (ii) the use of divalprex sodium and (iii) the administration of said composition in various dosage delivery systems including intransally, intracranially, transdermally, a sustained release formulation, liposome formulation, by implantation of a formulation or therapeutic device.

However, one having ordinary skill in the art would have known by the art-recognized routine knowledge (Levin Bentley and Becker) that determination of various dosage delivery system or dosage formulation including intranasal, intracranial or transdermal delivery or sustained release formulation, liposome formulation or by implantation or therapeutic device is well within the skill of artisan, especially in migraine therapy art. Furthermore, one having ordinary skill in the art would have expected that the incorporation of divalproex sodium would provide beneficial effect to the treatment of migraine headache. It is obvious to combine two or more compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. *See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).* One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

With respect to the incorporation of hyperosmotic agent or solution, Becker teaches the use of mannitol as well known secondary agent for furosemide formulation. Thus, one having ordinary skill in the art would have been motivated to combine the references and make such modification to increase the efficacy and extend the usage of furosemide containing composition by making suitable formulation for the claimed invention to accommodate patient's preference and needs where the compliance could be improved with effective and well tolerated dosage regimen.

11. Claims 25-26, 33, 39-44 and 47-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over dePadova (US 5753651), and further in view of Levin (US 6432986) and Bentley et al. (US 6369094).

The teaching of dePadova has been discussed in above 35 USC 102(b) rejection.

Levin is being supplied as a reference to demonstrate the routine knowledge in the art of delivering anti-migraine agents by intranasal and transdermal or topical administration (column 36, lines 31-38; column 9, lines 7-17; column 41, lines 40-43); sustained release formulation, liposome formulation (column 31, lines 22-31); by implantation or therapeutic device (column 39, lines 3-62).

Bentley is being supplied as a reference to demonstrate the routine knowledge in the art of delivering anti-migraine agents in various dosage forms including oral, intracvernosal, parenteral (i.e., intracranially), transdermal, ocular and topical administration or controlled released and fast dispersion formulation (column 3, line 8 thru column 4, line 60).

The teaching of dePadova differs from the claimed invention in (i) the incorporation of a blood brain barrier permeability enhancer or hyperosmotic agent or solution (claims 25-26, 33, 39, 40 and 53, (ii) the administration of said composition in various dosage delivery systems including intransally, intracranially, transdermally, a sustained release formulation, liposome formulation, by implantation of a formulation or therapeutic device.

However, one having ordinary skill in the art would have known by the art-recognized routine knowledge (Levin Bentley and Becker) that determination of various dosage delivery system or dosage formulation including intranasal, intracranial or transdermal delivery or

sustained release formulation, liposome formulation or by implantation or therapeutic device is well within the skill of artisan, especially in migraine therapy art.

12. Claims 25-26, 33 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathew et al. (Neurology, 1996;46:1226-1230) in view of Read et al. (Cephalalgia, 1997, December, 17(8):826-832).

The teaching of Mathew has been discussed in above 35 USC 102(b) rejection.

Read teaches use of furosemide in non-reactive carrier or hyperosmotic agent such as saline solution, which is a loop diuretic with activity at the electroneutral Na+K+2CL-, in inhibiting regenerative cortical spreading depression in anaesthetized cats, wherein the mechanism of inhibition of cortical spreading depression activity by furosemide may be through alterations in cortical ion buffering capacity or inhibition of cell swelling in neurons or glia (abstract; page 826, column 1, para. 1-3 thru column 2, para. 1; page 837, column 2, para. 2). Read also teaches that the inhibition of cortical spreading depression is potentially useful for the treatment of migraine therapy (abstract; page 832, column 1, lines 7-11).

The teaching of Matthew differs from the claimed invention in the use of said Na+K+2Cl- as only agent that materially affect the basic and novel characteristic of the claimed invention. To incorporate such teaching into the teaching of Mathew, would have been obvious in view of Read who teaches the use of furosemide as potential agent for the treatment of migraine therapy. One having ordinary skill in the art would have expected as taught by Read that furosemide alone could be useful for the treatment of migraine therapy. One having ordinary skill in the art would have been able to make correlation between Matthew's teaching in the activity of furosemide in enhancing the efficacy of abortive antimigraine agent and Read's

teaching in using furosemide as a potential agent for the migraine therapy. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 21, 25-29, 33 and 36-37, 39-45, 47-53 and 56 are provisionally rejected under the judicially created doctrine of double patenting over claims 12-18 of copending Application No. 11/101,000. are provisionally rejected under the judicially created doctrine of double patenting over claims 12-18 of copending Application No. 11/101,000. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the copending application and the instant application overlaps to each other. Since the instantly claimed "migraine headaches" falls under the term

"neuropsychiatric disorder", the copending application makes obvious the instantly claimed composition.

Response to Arguments

14. Applicant's arguments filed November 07, 2005 have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that the presently claimed methods reciting language of "consisting essentially of" is not taught in the Mathew.

This argument is not found persuasive. Unlike the applicant's argument, the instantly claimed methods reciting "consisting essentially of administering an effective amount of a Na+K+2Cl-" does not limit the Na+K+2Cl- as the sole active ingredient in the final composition Since "consisting essentially of" language is placed before "administering" language, the interpretation of the instant claims does not allow for the exclusion of any other unspecified ingredients in said composition. It is clear in reading the dependent claim 28 that the claimed composition may contain the additional active ingredients such as "anticonvulsants and non-steroidal anti-inflammatory". Therefore, the referenced method "metes and bounds" the claimed invention.

Applicant's argument in the response takes the position that the December 1997 issue of Cephalgia was not received by any subscriber on or before the December 23, 1997 priority date of the present application, and that the Read et al. reference is therefore not prior art to the present application.

This argument is not found persuasive. As discussed in the Office Action mailed July 26, 2004 (page 13), Cephalalgia is published 8 issues/year excluding January, March, July and

September, usually in the first week of month, and delivers to the subscriber. Although applicant provides the library receival date of the December issue of the article (January 6,1998), such showing cannot be considered as overcoming evidence for 35 USC 102(b) rejection since it is not same as the publication date. Therefore, considering the usual monthly publication date of the article, the communication between authors and editors (Received 28 May 1997, accepted 12 September 1997) and the absence of evidence to the contrary, the examiner maintains that the Read et al. references qualifies as the prior art to the present application.

Applicant's argument in the response takes the position that the Mathew does not teach or suggest that administration of furosemide and/or acetazolamide in the absence of conventional anti-migraine agents would be effective in relieving the symptoms of migraine.

This argument is not found persuasive. As discussed above, there is no indication in the claims that Na+K+2Cl- must be present as the sole active ingredient in the claimed composition administering for the purpose of treating migraine headaches and symptoms of migraine headache. Rather, the interpretation of the instant claims still allow for the inclusion of any other unspecified ingredients in said composition. It is clear in reading the dependent claim 28 that the claimed composition may contain the additional active ingredients such as "anticonvulsants and non-steroidal anti-inflammatory". Although the applicant amended the claims to recite "consisting essentially of ", that does not limit the Na+K+2Cl- as the sole active ingredient in the final composition as discussed above.

No argument pointing out disagreements with the examiner's provisional rejection of the claims under the judicially created doctrine of double patenting is present. Thus, the examiner maintains that the claims 21, 25-29, 33 and 36-37, 39-45, 47-53 are provisionally rejected under the judicially created doctrine of double patenting over claims 12-18 of copending Application No. 11/101,000.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. No Claim is allowed.

17. `Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
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